Claims

What is claimed is:

1. A method for altering the load of a Hepatitis virus in a host organism infected with said virus, comprising the modulation of the complex formation of a heterogeneous nuclear ribonucleoprotein (hnRNP) K or a functional fragment thereof with a regulatory region on the Hepatitis virus genome.

2. The method of claim 1, wherein the said virus is selected from the group consisting of mouse Hepatitis virus, woodchuck Hepatitis virus, ground squirrel Hepatitis virus, arctic ground squirrel Hepatitis B virus, human Hepatitis B virus (HBV), duck Hepatitis B virus, heron Hepatitis B virus, sheld goose Hepatitis B virus, snow goose Hepatitis B virus, Ross' goose Hepatitis B virus, stork Hepatitis B virus, woolly monkey Hepatitis B virus, orangutan Hepadnavirus, GB virus B, and human Hepatitis C virus (HCV).

3. The method of claims 1 or 2, wherein the host organism is a microorganism or a mammal.

4. The method of any of claims 1 to 3, wherein the mammal is selected from the group consisting of a rat, a mouse, a squirrel, a hamster, a woodchuck, an orangutan, a woolly monkey, a chimpanzee, a tamarin (*saguinus oedipus*), a marmoset and a human.

5. The method of any of claims 1 to 4, wherein the modulation of said complex formation is achieved by means of altering the total amount of a variant of heterogeneous nuclear ribonucleoprotein (hnRNP) K or a functional fragment thereof in the cell.

6. The method of any of claims 1 to 5, comprising administering a compound that modulates the complex formation of a hnRNP K protein or a functional fragment thereof with the regulatory region on the Hepatitis virus genome.

7. The method of any of claims 1 to 6, wherein the regulatory region is enhancer II of a hepadnavirus.

8. The method of claim 7, wherein the enhancer II region comprises positions 1554 to 1645 of the Hepatitis B virus genome.

9. The method of any of claims 1 to 8, wherein the said virus is the human Hepatitis B virus.

10. The method according to any of claims 1 to 9, where the method is an in-vivo method for the identification of suitable compounds that modulate said complex formation.

11. The method of claim 10, comprising administering a suitable compound for modulating the complex formation of a hnRNP K or a functional fragment thereof protein with the regulatory region on the Hepatitis virus genome.

12. The method of claim 11, further comprising measuring the number of Hepatitis virus particles in the host organism over a period of time.

13. The method of claim 11 or claim 12, further comprising:
comparing the obtained results with those of a control measurement.

14. The method of claim 13, wherein the control measurement comprises the use of a compound that does not modulate the complex formation of said hnRNP K protein or a functional fragment thereof with the regulatory region on the Hepatitis virus genome.

15. The method of claim 13, wherein the Hepatitis virus is the human Hepatitis B virus, the regulatory region is enhancer II, and wherein the control measurement comprises the use of a variant of HBV that does not contain adenine at position 1752 of the virus sequence.

16. The method of any of claims 1 to 3 and 5 to 15, wherein the host organism is a recombinant microorganism expressing a hnRNP K protein or a functional fragment thereof.

17. The method of claim 15, wherein the microorganism is a cell derived from liver tissue.

18. The method of claim 17, wherein the cell is of or derived from a hepatocellular or a hepatoblastoma cell line.

19. The method of claim 18, wherein the cell line is selected from the group consisting of HepG2, Hep3B, HCCM, PLC/PRF/5, Sk-Hep-1, Snu182, HuH-6 or HuH-7.

20. A method of any of claims 1 to 19, wherein the complex formation of the hnRNP K protein or a functional fragment thereof with the said regulatory region of the Hepatitis virus is reduced by means of a nucleic acid molecule.

21. The method of claim 20, wherein the nucleic acid molecule is RNA or DNA.

22. The method of claim 21, wherein the nucleic acid molecules is an aptamer, a micro RNA (miRNA) molecule or a small interfering RNA (si-RNA) molecule.

23. The method of claim 22, wherein the nucleic acid molecules is a si-RNA molecule comprising the sequence of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8 or SEQ ID NO: 10.

24. A method of any of claims 1 to 23, wherein the interaction of a hnRNP K protein or a functional fragment thereof with a regulatory region of the Hepatitis virus is modulated by a compound that modulates the phosphorylation status of cellular components.

25. The method of claim 24, wherein the compound alters the degree of phosphorylation of a hnRNP K protein or a functional fragment thereof.

26. The method of claim 24, wherein the compound alters the intracellular quantity of hnRNP K proteins or functional fragments thereof.

27. The method of any of claims 24 to 26, wherein the compound is an agonist or antagonist for a molecule on the cell surface.

28. The method of claim 27, wherein the molecule on the cell surface is a receptor.

29. The method of claim 28, wherein the receptor is a receptor tyrosine kinase, a membrane receptor with associated tyrosine kinase activity, or a G protein coupled receptor.

30. The method of claim 29, wherein the receptor is a receptor for a platelet derived growth factor, a receptor for erythropoietin, a receptor for tumor necrosis factor, a receptor for leukaemia inhibitory factor, a receptor for an interferon, a receptor for insulin, a receptor for an insulin-like growth factor, a receptor for an interleukin, a receptor for a fibroblast growth factor, a receptor for a granulocyte-macrophage colony stimulating factor, a receptor for a transforming growth factor, or a receptor for an epidermal growth-factor.

31. The method of any of claims 27 to 30, wherein the agonist or antagonist is a protein.

32. The method of claim 31, wherein the protein is a mutein based on a polypeptide of the lipocalin family, a glubody, an immunoglobulin or a protein based on the ankyrin or crystalline scaffold, binding to a receptor tyrosine kinase.

33. An in-vitro method of identifying a compound capable of altering the formation of a complex between a hnRNP K protein or a functional fragment thereof, and a Hepatitis virus or a functional fragment thereof that contains the enhancer II region, comprising contacting the components that form said complex with each other.

34. The method of claim 33, comprising:

(a) adding a compound to the test tube that modulates the complex formation of said hnRNP K protein or a functional fragment thereof with the enhancer II regulatory region on the Hepatitis virus genome, and

(b) detecting the said complex formation.

35. The method of claim 34, wherein the detection is performed by a suitable spectroscopic, photochemical, photometric, fluorometric, radiological, enzymatic or thermodynamic method, or is based on cellular effects.

36. The method of claim 35, wherein the photochemical method comprises a cross-linking reaction.

37. The method of claim 35, wherein the spectroscopic method comprises the use of fluorescence correlation spectroscopy.

38. The method of claim 35, wherein the photometric detection method comprises the use of a label that is optically detectable.

39. The method of claim 35, wherein the radiological detection method comprises the use of a radioactive label.

40. The use of claims 38 or 39 that comprises the use of an electrophoretic mobility shift assay.

41. The use of any of claims 33 to 40 comprising the use of at least two nucleic acid molecules comprising the enhancer II region of the Hepatitis B virus DNA sequence, one of which does not contain adenine at position 1752 of the said sequence.

42. The method of claim 41, wherein the nucleic acid molecule not containing adenine at position 1752 is used for a control measurement.

43. The method of any of claims 33 to 42 for the in-vitro screening for potential compounds that are useful for treatment of Hepatitis infection due to their inhibition of the complex formation of a hnRNP K protein or a functional fragment thereof with a Hepatitis virus, comprising the simultaneous screening of compound libraries on multiple-well microplates using automated work stations.

44. The method of claim 43, wherein the Hepatitis infection is caused by HBV.

45. The use of a compound selected from the group consisting of aptamers, micro RNA molecules, small interfering RNA molecules, compounds that modulate the absolute quantity of hnRNK proteins in a cell, compounds that modulate the degree of phosphorylation of hnRNP K proteins, and agonists or antagonists for a cell surface receptor that is able to induce the regulation of a cellular kinase or phosphatase, for the manufacture of a medicament for the treatment of Hepatitis infection, wherein the viral load is altered via the modulation of the complex formation of a hnRNP K protein with a regulatory region on the Hepatitis virus genome.

46. The use of claim 45, wherein the agonist or antagonist for a cell surface receptor that is able to induce the regulation of a cellular kinase or phosphatase is a mutein

based on a polypeptide of the lipocalin family, a glubody, an immunoglobulin or a protein based on the ankyrin or crystalline scaffold, binding to a receptor tyrosine kinase, a membrane receptor with associated tyrosine kinase activity, or a G protein coupled receptor.

47. The use of a compound identified by a method of any of claims 8 to 44 for the manufacture of a medicament for the treatment of Hepatitis infection, wherein the viral load is altered via the modulation of the complex formation of a hnRNP K protein with a regulatory region on the Hepatitis virus genome.

48. The use of any of claims 45 to 47, wherein the Hepatitis infection is caused by HBV.

49. The use of a compound selected from the group consisting of aptamers, micro RNA molecules, small interfering RNA molecules, compounds that modulate the absolute quantity of hnRNK proteins in a cell, compounds that modulate the degree of phosphorylation of hnRNP K proteins, and agonists or antagonists for a cell surface receptor that is able to induce the regulation of a cellular kinase or phosphatase, for the manufacture of a composition for the diagnosis of Hepatitis infection.

50. The use of claim 49, wherein the agonist or antagonist for a cell surface receptor that is able to induce the regulation of a cellular kinase or phosphatase is a mutein based on a polypeptide of the lipocalin family, a glubody, an immunoglobulin or a protein based on the ankyrin or crystalline scaffold, binding to a receptor tyrosine kinase, a membrane receptor with associated tyrosine kinase activity, or a G protein coupled receptor.

51. The use of a compound identified by a method of any of claims 8 to 44 for the manufacture of a composition for the diagnosis of Hepatitis infection.

52. The use of at least two nucleic acid molecules comprising the enhancer II region of the Hepatitis B virus DNA sequence, one of which does not contain adenine at position 1752 of the said sequence, for the manufacture of a kit or a composition for use in evaluating Hepatitis infection.